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THE UNIVERSITY OF TORONTO MEDICAL JOURNAL

(An Undergraduate Publication)

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EDITORIAL

MEDICAL LIBRARY FACILITIES.

Though many of the departments of the Faculty of Medicine have developed excellent libraries for their particular subjects, the main Medical Reading Room is proving inadequate. Especially is this true for the student in his clinical years, away from the campus.

Apparently, the tendency is towards the development of departmental libraries, such as those in Physiology, Hygiene, Biology, Psychology, Pathology, and Paediatrics. These are well equipped though usually with large donations from the professors of the respective departments. The libraries keep in touch with the literature and are most helpful in selecting reading material and finding articles. Especially is this so at the Academy of Medicine, where final year students are admitted by courtesy.

That the main library is inadequate is probably due to two reasons—location and regulations, the latter probably being the greater. In order to borrow a book for overnight use, one must call in the morning, before any of his rivals, to sign for it,call again at night to get it, and once more walk up to the library to return it next morning. To serve those whose day is so completely filled as that of the medical undergraduate, such a system is hopeless. The Medical Reading Room is a comparatively new section of the University Library, but until the authorities realize that regulations suitable for all colleges are not applicable

to Medicine, it will not be a success. The twelve or fourteen hours of lectures per week of the Arts man, and the proximity of the Library to the main lecture rooms, make it possible that books can be signed for, called for and returned next morning on threat of a twenty-five cent fine. A trip to the Library means twenty minutes at least to the undergraduate taking clinics at the nearest hospital—this, three times for one book, is an hour; and twenty-five cents fine because he cannot return the book before noon unless lectures or clinics are missed. Ardent, indeed, is the soul who would use our University Medical Library.

The contents of the shelves are being rapidly improved in many subjects. The shelves on Anatomy and Biochemistry appear particularly well laden. The periodicals received appear to be the best collection for which one could hope. But the books to be found on certain subjects appear woefully inadequate, especially in Otolarynology, Ophthalmology, Therapeutics — perhaps many others, but the blanks will be filled in by any student who has tried to use the Library.

It was most unfortunate that the period before Christmas was chosen to try opening the Medical Reading Room in the evenings. Of course people did not go. Medical students just don't work then—at least not in libraries. But from now on there will be hundreds who would use the Reading Room if they could—writing theses and articles, studying for examinations, reading journals and monographs. Medical students must do all their reading in the evenings, for that is all the time they have by the time-table. All medical libraries are closed by six o'clock. Let not anyone criticize the narrowness of an undergraduate's knowledge till opportunities for library service are afforded. If the University Library cannot be improved, the building-up of departmental libraries, especially of the beautiful room on the 3rd floor of the Banting Institute, where the clinical subjects could be housed, appears to be one solution.

THE ARTICLES ON ACUTE APPENDICITIS AND BRIGHT'S DISEASE.

It is regretted that the second papers on Acute Appendicitis and Bright's Disease have been omitted from this issue of the Journal, but it is hoped that they will be available for next month.

GOING-TO-PRESS DATES.

In an effort to bring out the Journal before lectures are over this Spring, those intending to write papers for the April and May numbers are requested to submit their articles to their editorial representatives before March 10th and April 1st respectively. The Editors will welcome papers on any subject of medical interest, and suggest that prospective authors submit their papers at the earliest possible date.

APPOINTMENTS TO THE JOURNAL STAFF.

Applications for positions on the Journal Staff for 1932-33 will be received until April 1st, 1932. The following positions will be open to applicants:

Year Representatives for each of the five years.

Editorial Representatives for each of the 2nd and 3rd years, and from the last three years (for special writing).

Assistant Editor, from the incoming fifth year, and Assistant Managing Editor.

It is hoped that those who are particularly interested in the Journal, and in writing for it, will apply, stating any experience and special interests, such as Book Reviews, advertising, circulation, etc. It is apparent that it would be to the benefit of all, if future editors had experience in the management of the Journal. The Editorial Board will consider all applications carefully, but will not necessarily accept any of them.

Applications should be addressed to the Editor, University of Toronto Medical Journal, Room 107, Anatomy Building.

A Continuing Partnership.*

By J. G. FITZGERALD, M.D.
Dean of the Faculty of Medicine.

It is with pleasure that I embrace the opportunity afforded me upon this occasion of addressing a few observations to the members of the graduating class in medicine.

It has seemed to me that certain mutual advantages might accrue if undergraduates and graduates in medicine were thought of as one set of partners, and their instructors and subsequent professorial colleagues were conceived of as the other members of a partnership. That we may more satisfactorily examine the possibilities inherent in such relationship, it is incumbent upon us at the outset to retrace our steps and observe or recall the events which led up to this potentiality of partnership. Fresh in your minds are the days not long past when your studentship and apprenticeship in medicine began. The path which you chose in the autumn of 1926 you have doubtless already found, has on it numerous obstacles which have served to challenge your ingenuity and resourcefulness, your interest and your intelligence. There have been times, too, when it may have seemed to many of you that disillusionment must certainly be just around the corner. Indeed, in respect to many of the hopes and ambitions cherished in one's undergraduate days, it is perhaps a matter for congratulation later that they have sunk deeply into the subconscious and having lost their earlier significance, do not emerge subsequently. The mechanism of such mental operations you have become aware of through experience, which possibly has been supplemented by the knowledge of psychology you have acquired.

But we must not linger, because at this moment we are concerned only with the preparation which your course has afforded you to equip and qualify yourself for the real business of satisfactory partnership, which we are to further elucidate. As you passed from your junior years, it has become clear to you, I am sure, that those with whom you are to co-operate, and under whose guidance and direction you are being prepared for your life work, have been wise in providing you with very substantial intellectual fodder during your primary years. You will not have progressed far in your clinical studies before becoming aware of the essential need of thorough preparation in the biological sciences, and very especially physiology, if you are to make anything of the extraordinary puzzles which confront you as you proceed with your clinical work. The exceedingly interesting mysteries hidden in cases of profoundly disturbed metabolism; of obscure infections; in the end-results of long continued exposure to noxious agents; from obscurity as to the cause of sudden death in acute infection—will have brought home to every one of you clearly, that even the extended courses of study of biochemistry, physiology, pharmacology, bacteriology and pathological chemistry have really been wholly inadequate to ensure solution by you of many obstetrical, medical and surgical problems. After quiet reflection you will realize that a very broadly conceived, scientific preparation was not only wise, but in addition a vital necessity. If some of these things presently seem to lack reality, given time, I have no doubt that you will esteem, as I do, such preparation very highly.

Now we may assume for the purpose which we have in view at the moment that you have reached the end of your undergraduate period and are ready to

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* Address to the Graduating Class in Medicine, University of Toronto, delivered February 6, 1932.

undertake the tasks for which ultimately you will be obliged to assume entire responsibility. I would not have you think that the partnership thus far has been one in which there have not been credits and debits on both sides. Some of your instructors have given much more than they have received, and you are heavily in their debt. Others, for various reasons, may be in an almost evenly balanced state, having given much or little, and having received in like measure. And now it may be that for many of you, your immediate contact with those who have endeavoured to guide and inform and assist you, will cease. With many more it is to continue for a little time, perhaps for one or several years. But since perhaps two-thirds of the class at least will be engaged in the practice of medicine in this city or in the Province of Ontario or elsewhere in Canada, it is almost certain that more or less continuous and active association will be maintained. And even for those who go elsewhere, to the United States or other countries, I am sure we of the Faculty feel, and I trust you of the student body do also, that upon every occasion which may present itself of continuing, and, if possible, of intensifying mutually helpful relationships, these will be embraced.

After all, you as medical graduates can do much not only to benefit yourselves individually, but, what is even more important, to make it apparent that you have a keen appreciation of your social obligations and of the fact that your native province (or the community in which you have been privilleged to pursue your undergraduate medical studies), has not hesitated to assume heavy financial burdens that you might acquire your necessary professional equipment.

And what do I mean by this last statement? Simply this—that the actual cost of medical education in the modern, well equipped, well organized medical faculty, far exceeds the sums which students are required to pay in the form of fees for attendance upon the course offered. It may be twice, it may be three times the amount which the University collects that is required to meet the cost of each and every medical student enrolled. And that is only one part of the story. It is to be recalled that in all the laboratory as well as in the various clinical departments, a very large proportion of the staff engaged in giving instruction, do so at their own expense and in their own time. Many of them receive honoraria, which are thus described, in the pious hope that their recipients will not ponder, much less fully realize, their inadequacy. Those so engaged make no complaint. Hours in hospital wards, similar long periods of time in laboratories both in the pre-clinical and clinical years of your course have been spent, not by a few, but by literally dozens of those whom we collectively describe as the Faculty. Furthermore, there are those who, upon one or more occasions, without even academic recognition, do what lies in their power to acquaint you with facts which may be useful to you as medical practitioners.. As an illustration, I may cite the fact that in the field and practical course in Hygiene and Preventive Medicine, between 30 and 35 persons freely and generously give of their time to assist in the conduct of that course, and their reward is the satisfaction which comes from work well done and a letter of thanks from the head of the department. These are two kinds of debits in the mythical ledger which we have opened on your behalf. And then there is another and more important one. It is this. Very especial opportunities and privileges have been yours. The organized community has provided hospitals to which you have had access. Sick persons have generously permitted you not infrequently to observe and examine them that their various symptom pictures might become fixed in your minds. This sort of obligation is a very unusual one, and perhaps not sufficiently appreciated. Then again, your country and this Province of Ontario have made very generous legal

provision to safeguard you, once you are launched upon your professional career. When you have completely satisfied the requirements of the medical curriculum and emerge from the obstacle races, usually designated examinations, of the licensing bodies, you will find that your rights and privileges are indeed exceptional. Is it surprising that organized society very properly expects in return that you will appreciate that you have obligations which are not shared by others engaged in professional endeavours or tasks of many kinds which have not necessitated the expenditure of large sums of public moneys for the preparation of those engaged in them? This, I would suggest to you, is almost your largest and most serious single debit.

Once launched upon the practice of medicine, or perhaps engaged in some special field of medical endeavour other than practice, your opportunity has arrived to begin piling up credits. This you may do in a variety of ways. In joining your local, provincial and national medical organizations, you will give more than you will receive, and, incidentally, this particular undertaking offers one of the best of many opportunities for continuing friendly intercourse and association with your former instructors and, as I hope, continuing partners. Under the admirable arrangements presently existing whereby the Canadian Medical Association and the Ontario Medical Association, with the assistance and co-operation of the faculties of this and other universities, provide extra-mural, post-graduate medical instruction, every effort is made to keep you fully abreast of all new developments in the field of general medicine which may be of value to you in the conduct of your daily work. Individually or in teams, instructors proceed to local centres, particularly to those in outlying places, if possible one in which there is a hospital, to give clinics and lectures and to hold informal conferences where a great variety of every-day problems arising in medical practice may be discussed and, if possible, their solution found. It will be evident upon reflection that in this matter it may well be felt that more than credits are to be secured. However that may be, I can assure you that those engaged in this work have a very real and continuing sense of their obligations and opportunities and spare no effort to realize them.

In another field some of your colleagues and co-partners in this business of affording the community sound scientific medical advice and service, are valuable for collaboration with you in quite different undertakings. States and provinces, cities and towns, and in some instances combinations of municipalities, have set up services for the protection of the public health. In these organizations qualified medical and other scientific personnel are prepared and equipped to share with you fruitful advantages inherent in a partnership based upon good-will and community of interest. Physicians are prepared to aid you in the diagnosis of difficult cases of communicable diseases, and others are trained that they may undertake on your behalf (and through you that of your patients) various bacteriological, serological, chemical and other examinations which will give you additional and often much needed information, so that you may the more readily arrive at a correct diagnosis or prognosis. In this same field, engineers, statisticians, and public health nurses are co-opted by your medical confreres to augment the value of the service which they endeavour to render.

Now, may I take a moment to direct your attention to still another field of work in which problems much more subtle and difficult of solution are encountered and where it is especially necessary that you have wise and experienced partners to collaborate with you?

I have in mind the field of mental medicine. Problems of abnormality, subnormality, maladjustment, anti- social attitudes and anomolous behaviour may indeed lead you to be very grate-

ful when you realize that you may turn to those working in the field of psychology and psychiatry to come to your assistance when you find yourself with problems which are far from easy of solution. You may receive most valuable aid from your former instructors whose lives are spent in dealing with patients who present few, if any, physical signs of disease, but who, nevertheless, are utterly incapable of satisfying the requirements of their environment and are a heavy burden to themselves, to their families, to their physicians and to society at large. In this domain, perhaps more than in any other, you will be glad to have the counsel and advice of those suitably equipped to provide it.

I cannot, if I would, illustrate all the many and varied opportunities which exist for useful team-work between you and your fellow-practitioners and former students on the one hand, and that body of men who at the present and in the past have, to the best of their ability co-operated to set before you in laboratory, in clinic, in the out-patient department, in the lecture room, your opportunities in that vast domain which we label scientific medicine. That it may not be imagined that I have overlooked the advantages which have accrued to you from the contact with your fellows in other faculties and colleges and from the opportunities of association in extra-curricular activities, I have only to remind you that during the course which you have pursued, whether purely medical or a combined course in arts and medicine, there have been provided by your university, opportunities for you to gain an insight into wholly non-technical and non-professional activities; to hear good music; to see worth-while exhibitions of art in its many forms; to devote yourself to the cultivation of avocations, to the end that you may be well-rounded persons with broad and intelligent interests. In other words, your partners have endeavoured to acquaint you with the ideals and the steps which must be taken to acquire true education, the end of which has been eloquently described by Huxley as follows:

> "That man, I think, has had a liberal education, who has been so trained in youth that his body is the ready servant of his will, and does with ease and pleasure all the work that as a mechanism it is capable of; whose intellect is a clear, cold logic engine, with all its parts of equal strength, and in smooth working order; ready, like a steam engine, to be turned to any kind of work, and spin the gossamers as well as forge the anchors of the mind; whose mind is stored with a knowledge of the great and fundamental truths of nature and of the laws of her operations; one who, no stunted ascetic, is full of life and fire, but whose passions are trained to come to heel by a vigorous will, the servant of a tender conscience; who has learned to love all beauty, whether of nature or of art, to hate all vileness, and to respect others as himself.
>
> Such an one and no other, I conceive, has had a liberal education, for he is, as completely as a man can be, in harmony with nature. He will make the best of her, and she of him. They will get on together rarely; she as his ever-beneficent mother; he as her mouth-piece, her conscious self, her minister and interpreter."

To realize this obviously means that you and we, the partners, must continue to be students all our lives, eagerly endeavouring to extend the boundaries of knowledge in our own fields; to add to the amenities of that social organization of which we are all a part; and finally, to strive in every way to justify our inclusion in such a splendid partnership.

The Fellowship of the Royal College of Surgeons of England.

By PROF. WILLIAM WRIGHT, M.D., D.Sc., F.R.C.S.,

Dean, London Hospital Medical College, University of London.
Examiner in Anatomy for the Fellowship.

"To the making of many books there is no end"; the same might be said of the making of diplomas. As, however, there are books and books—the biblia abiblia of Charles Lamb—so there are diplomas and diplomas. Among diplomas it is safe to say that none stands higher than that of Fellow of the Royal College of Surgeons of England, which for many years has held an unrivalled position among the surgical diplomas or degrees of Great Britain. The possession of it is now regarded as practically obligatory for membership of the honorary staff of all the hospitals connected with the medical faculties of the English Universities. It may be of interest to learn how the diploma came into existence and how it may be obtained, but first a few words about the Royal College itself.

Although the Charter of the College only dates from 1800, the Charter descends from an earlier Charter granted by Edward IV. as far back as 1462, to the Freemen of the Mystery of Barbers in the City of London, practising Surgery. Before the date of this earlier Charter there were two Guilds exercising authority in London in matters relating to the practice of Surgery—the Barbers' Guild of which we first hear in 1308, and a rival Surgeons' Guild, mentioned in the City Records of the year 1369. By a charter of Henry VIII. the two Guilds became united, an open and visible sign of the union being the joint occupancy of Barbers' Hall, which still stands on its old fifteenth century site in Monkwell Street. The union, never we may imagine a very happy one, was dissolved in 1745, the surgeons finding a new home in Surgeons' Hall in the Old Bailey, entering into possession in 1751.

The grant of the Charter of 1800, to which reference has previously been made, whereby the name of the Royal College of Surgeons in London was first authorized, was probably hastened by the Company of Surgeons, which had recently acquired a freehold site in Lincoln's Inn Fields, being entrusted with the care of the Hunterian Collection of Museum Specimens.

In 1843 still another Charter was granted whereby the name of the College was changed to that of the Royal College of Surgeons of England and a new class of members was instituted who were to be known as Fellows, from and by whom the Council was to be elected. "The first Fellows, three hundred in number, were chosen mainly from the Surgeons, Assistant Surgeons, and Lecturerers of the Metropolitan and Provincial Hospitals. They were elected under one general diploma on December 11th, 1843. A further election of two hundred and forty-two Fellows took place on the 26th August, 1844, and these included a considerable number of representatives of the Naval, Military and Indian Forces."*

The first examination for the Diploma of Fellow was held in December, 1844. It lasted two days, the first day being devoted to the subjects of Anatomy and Physiology, the second to those of Pathology, Therapeutics and Surgery. The examination in Anatomy and Physiology was made a separate examination with the distinguishing title of "the Primary Examination," under a by-law passed in 1874. The first Primary examination under these new conditions took place in May, 1876. At the present time there are between 2,000 and 2,100 Fellows.

*The above statement is taken from an Historical Summary in the Calendar of the College, a Summary to which I am generally much beholden).

The Primary and Final examinations are each held twice a year in London; the Primary in the early part of June and December, the Final in the later part of May and November. In 1929 a Primary examination was held in Toronto, in 1930 in Montreal, in 1931 in Melbourne and Toronto, these being the only occasions on which the examination has been so far held outside London.

Although at the Primary examination the candidate may be asked questions on any subject which may be fairly regarded as lying within the broad fields of Anatomy including embryology, and of Physioloy including histology and bio-chemistry, special attention is given to such matters as have an important bearing on the surgeon's art. The examination consists of written and oral portions, there being four questions in the Anatomy paper all of which must be answered, and six questions in the Physiology paper of which four only are to be answered. The questions set at past examinations are published by Taylor and Francis, Red Lion Court, Fleet St., London, E.C.4, from whom they are obtainable for a small sum. The oral portion of the examination extends over a period of forty minutes, twenty minutes being devoted to each of the two subjects. Although there are no fixed rules as to how this portion of the examination shall be conducted, it is a common practice to spend a considerable part of the time available in Anatomy, on Osteology and in Physiology on Histology. In Anatomy the candidate is examined in addition upon dissected bodies, upon dissected parts on trays or in bottles and upon the living model; in Physiology upon such matters as the chemical composition of various body fluids, upon the use of various physiological instruments and upon tracings of the movements occurring in the circulatory and respiratory systems. I would add that occasionally questions are asked in both the written and oral portions of the anatomy examination on morphology should a knowledge of them serve to explain some embryological condition or illustrate some biological principle. The standard of knowledge required from the candidate is high, only something like thirty per cent. of the candidates who present themselves for examination are usually successful; on the other hand the examination is one in which a candidate who is well prepared has an excellent prospect of passing, provided he retains his composure. As to preparation for the examination there is no better way than by acting as a student demonstrator in one or other subject, or still better in both, an experience which should ensure not only a sound practical knowledge of the subjects, but also engender that sense of confidence so essential for success in all examinations. In the absence of such opportunities, the candidate should spend as much time as possible with forceps and scalpel in the dissecting room, and with test tubes and reagents in the physiological laboratory.

The final examination has never been held away from London, nor is it likely that it ever will be. The subject of examination is Surgery in all its branches —Surgical Anatomy, Surgical Pathology, Operative Surgery. The best preparation for this examination, a preparation which practically speaking is essential, is to have acted as a House Surgeon under able and experienced general surgeons.

While no doubt a student who wishes to obtain the diploma will have to engage himself deeply in the study of the subjects of the examination, he may be promised much pleasure in his pursuit of knowledge, as well as a reasonable prospect of ultimate success.

No diploma carries with it more honour or distinction, an opinion fully confirmed by the increasing number of candidates presenting themselves for it, canadidates gathered from all quarters of the Empire.

The Autonomic Nervous System.

By D. Y. SOLANDT, M.A., '33.

The study of the physiological phenomena involved in the control of the internal environment of the animal body has left science in no doubt concerning the importance of the role played by the autonomic nervous system. This group of neural pathways, so long the object of idle speculation, has, in the last decade, been granted its rightful place among the controlling elements of the biological mechanism.

In this short account of the salient features of the autonomic nervous system we will first consider the anatomical distribution and follow with the related physiological phenomena and the relevant pharmacological reactions. Such a discourse must, of necessity, be synoptic. It is hoped that sufficient clarity will be obtained to compensate for the great body of detail that must be omitted.

Anatomy.

The elements of the autonomic nervous system are arranged along the same lines as the neural structures of an ordinary spinal reflex arc of the central nervous system. The afferent neurone, say from an internal organ, proceeds to its cell station in a posterior root ganglion. From here the central process goes in to the grey matter of the spinal cord where its junction with the connector cell occurs. The position of the connector cell in the grey matter of the cord differs in the various regions. The connector cell must join the afferent neurone with the efferent or effector neurone, and this latter, unlike the analagous case in the spinal reflex arc of the central nervous system, lies outside the spinal cord. To reach the effector neurone the connector fibre from the connector neurone passes out of the cord with the anterior spinal root of the segment in which it lies. It proceeds in the mixed spinal nerve, and finally leaves the anterior division to form what we call the white ramus communicans. This ramus makes its way to the effector neurone, which may lie in one of the ganglia of the lateral sympathetic trunk adjacent to the spine, or peripherally in the substance or region of the organ supplied. When the effector, or, as it is sometimes called, the excitor cell lies in the lateral sympathetic trunk, its fibre leaves the trunk and joins the nerve, with which it is to be distributed, as the grey ramus communicans.

Very little is known about the afferent channels of the autonomic system. What knowledge we have relates mostly to the efferent pathway. Not all the segments of the central nervous system show efferent autonomic channels. Of the cranial nerves only the third, seventh, ninth, tenth and eleventh contain autonomic fibres. All the thoracic, the first two lumbar and the second and third sacral spinal nerves carry autonomic fibres.

The best classification of the autonomic system is based on the regions of origin of the efferent fibres from the central nervous system. Thus we get the cranial autonomic, the thoraco-lumbar autonomic and the sacral autonomic divisions. The cranial and sacral autonomic divisions constitute what is called the parasympathetic system. The thoraco-lumbar outflow of autonomic elements is known as the sympathetic system. Investigation shows that this anatomical classification is quite satisfactory from the standpoint of the known physiology of the system.

Cranial Division — Parasympathetic System.

(1) Third Nerve:—The autonomic fibres in this nerve are known as the midbrain outflow, in contrast to the bulbar outflow in the seventh, ninth, tenth and eleventh nerves

The connector cells for this outflow lie in the anterior portion of the occulo-motor nucleus, lying in the floor of the aqueduct of Sylvius. From here the connector fibres, after leaving the third nerve, make their way to the ciliary ganglion, where the effector cells are situated. The effector fibres pass to the ciliary muscles and the sphincter of the pupil in the short ciliary nerve, which also carries effector fibres from the sympathetic outflow.

(2) Seventh Nerve:—The connector cells lie in the dorsal nucleus, which is in line with the similar structures of the ninth and tenth nerves. This cell station is called the superior salivary nucleus. Connector fibres leave by the pars intermedia and reach the effector cells in the spheno-palatine (Meckel's) ganglion by way of the great superficial petrosal nerve. From here the effector fibres pass by the zygomatic nerve to the lacrimal gland, and by the palatine nerves to the unstriped muscle, vessels and gland substance in the palate and naso-pharynx.

The facial nerve carries other connector fibres which leave in the chorda tympani, join the lingual nerve, and end at effector cells in ganglia adjacent to the submaxillary and sublingual glands. These glands derive their secretory and vaso-dilator control from this source.

(3) Ninth Nerve:—The dorsal nucleus houses the small connector cells from which fibres arise and pass to the effector cells in the otic ganglion by way of the tympanic and the small superficial petrosal nerves. The dorsal nucleus is sometimes known as the inferior salivary nucleus since the effector cells in the otic ganglion supply the parotid gland with secretory and vaso-dilator fibres through the auriculo-temporal nerve.

(4) Tenth Nerve:—Here we know something of the afferent neurones which centre in cells stations in the ganglia of the neck and trunk. These fibres join the connector cells in the dorsal nucleus which lies in the floor of the fourth ventricle. This nucleus contains connector cells for both voluntary and involuntary neural pathways. The small autonomic connector cells are aggregated into the portion known as the nucleus intercalatus. From this region the connector fibres pass into the vagus nerve, and, in the substance of this nerve, reach the various viscera, still as connector cells. The effector cells are encountered in the substance or in the vicinity of each viscus.

The chief distribution of the vagus is to the heart and the intestinal tract, with lesser branches to the bronchi, kidney, liver, gall-bladder and pancreas. The effector cells in the heart are contained in the sino-auricular and auriculo-ventribular nodes and effector fibres are found in the bundle of His and its ramifications, and, to a lesser degree, in the musculature of both auricles and ventricles. In the alimentary tract the effector cells form what we call Auerbach's plexus. The control of the vagus extends from the oesophagus to the ileo-colic valve and probably for some distance up the ascending colon. The nature of the vagus control on the various organs will be discussed under the section dealing with the physiology of the system.

(5) Eleventh Nerve:—This nerve should be considered from the morphological standpoint as being one with the tenth nerve. Its dorsal nucleus is continuous with that of the vagus and a few small connector fibres, which join the vagus from the second and third cervical nerves, are thought to arise in this nucleus.

Sacral Division — Parasympathetic System.

The connector cells of this division lie in the lateral region of grey matter in the second and third segments of the sacral portion of the cord. Connector fibres are contained in the corresponding anterior roots, and, leaving this root, join to form the single pelvic nerve or nervus erigens on either side. The effector cells are found in the region or substance of each viscus sup-

plied, and over the bladder and rectum these cells form the pelvic plexus. The organs supplied are the bladder, the blood vessels of the penis, and the whole of the large intestine with the exception of the caecum and possibly a small part of the ascending colon.

The Sympathetic System.

As we have mentioned, this constitutes the thoraco-lumbar portion of the autonomic outflow, and shows all the neural elements of the autonomic reflex arc in their typical relationships. Associated with this group of nerve pathways, as a definite part of the sympathetic system, are the paravertebral and prevertebral ganglia.

The paravertebral ganglia constitute the lateral sympathetic trunk. There is a right and a left trunk, each running lateral and adjacent to the vertebral column. The ganglia are arranged segmentaly except in the cervical region, where we have only three, the superior, middle and inferior cervical ganglia. Elsewhere each spinal nerve has a corresponding ganglion in each trunk. Sometimes the last thoracic and first lumbar ganglia are fused to form the stellate ganglion. Over the coccyx the two trunks end in the ganglion impar, the result of the fusion of four coccygeal ganglia. Each trunk is made continuous by groups of nerve fibres running between the ganglia. The only connector fibres the trunks receive are those of the thoraco-lumbar outflow. In some cases the connector fibres join effector cells in the ganglia of the lateral sympathetic trunk, the effector fibres joining other nerve trunks as grey rami communicans. In other instances the connector fibres pass through the lateral trunk unchanged and proceed to effector neurones in the parts supplied or in the prevertebral ganglia.

The prevertebral ganglia enter into the formation of the four important prevertebral plexuses. Of these the cardiac plexus is placed at the base of the heart and receives branches from the sympathetic trunk by the superior, middle and inferior cardiac nerves. It also receives parasympathetic branches from both the vagi. The coeliac or solar plexus receives the greater splanchnic nerves, and from them its sympathetic connections. This plexus is divided into a right and a left part, each situated on the corresponding crus of the diaphragm and in close association with the aorta and the coeliac artery. The hypogastric plexus receives the hypogastric nerves, lies in the region of the bifurcation of the aorta, and may be considered as essentially a connecting link between the coeliac and pelvic plexuses. The pelvic plexus lies on either side of the rectum and over the bladder, and receives sympathetic fibres from the upper sacral ganglia of the lateral trunks. The parasympathetic connections to this plexus have been mentioned.

Sympathetic Distributions.

(1) Head and Neck:—The connector cells are situated in the second and third thoracic segments, and, after joining the lateral sympathetic trunk, proceed to the superior cervical ganglion where the effector cells are situated. Effector fibres pass to the eye by way of the coat of the internal carotid artery, the cavernous sinus, and probably the trigeminal nerve. Fibres go to the dilator muscle of the pupil, and to the smooth muscle retracting the upper lid, and to Muller's muscle which pushes the eyeball forward.

(2) Thoracic Viscera:—Connector cells are found in the third and fourth thoracic segments of the cord, and the fibres pass to effector cells in the three cervical sympathetic ganglia. Effector fibres pass to the lungs and heart by the sympathetic cardiac nerves.

(3) Fore-Limb:—The connector cells lie chiefly in the fifth to the ninth thoracic segments, from which points the fibres pass to the inferior cervical ganglion. Effector fibres, from the cells in this situation, are distributed with the nerves of the brachial plexus.

(4) Hind Limb:—The connector

cells are found in the last two thoracic and first two lumbar segments, and their fibres end at effector cells in the lowest lumbar ganglion in the lateral sympathetic trunk. Effector fibres are distributed to the lower limbs through the lumbo-sacral trunk.

(5) Abdominal Viscera:—The connector cells lie between the sixth thoracic and second lumbar segments. The connector fibres leave the sympathetic chain as the splanchnic nerves and join effector fibres in the vicinity or substance of the part supplied. Some connector fibres end in the coeliac and inferior mesenteric ganglia, from which points the effector fibres proceed along the larger arteries to supply the coats of the vessels themselves, and the organs which they reach.

The sympathetic system supplies fibres to the entire length of the large and small intestine, and probably to all the sphincters of the gastro-intestinal tract. The pyloric region, but not the body of the stomach, receives sympathetic fibres. All the vessels of the splanchnic area are supplied with vaso-constrictor fibres of the sympathetic. The kidney appears to derive vaso-dilator fibres from the sympathetic. The suprarenals, spleen, liver, and gall-bladder all receive fibres from the sympathetic. The ureters, uterus, fallopian tubes and vas deferens receive their total autonomic supply from the sympathetic. This includes both motor and inhibitor fibres, as the parasympathetic system sends no fibres to these organs.

(6) Skin:—The cutaneous supply to the head and neck is derived from excitor fibres passing from the superior cervical ganglion to the upper four cervical nerves.

The sweat glands, arrectores pili muscles, and the cutaneous capillaries and arterioles of the skin over the entire body receive sympathetic fibres. These fibres are distributed to the parts involved with the other sympathetic elements which we have treated under preceding headings.

Physiology.

To date our knowledge of the function of neural tissue is slight, and helps us very little in understanding the operation of the nervous system. Practically all the facts we possess in this connection are in the form of end results. Science is almost completely ignorant of the mechanisms whereby these results are brought about. For this reason we will have to limit this discussion to the functions, mostly as seen in overt phenomena, of the various divisions of the autonomic nervous system.

Sympathetic and Parasympathetic Systems.

The physiology of the afferent autonomic impulses is mostly centred around the contentious subject of referred pain. Normally the viscera, with the exception of the stomach, rectum and bladder, produce no sensory stimulation. Severe tension of a hollow viscus, due usually to internal pressure, will cause pain which will not be felt in the viscus itself, but rather at an area on the surface of the body, often distant from the origin of the afferent impulses. It is believed that the pain is interpreted as coming from the sensory area supplied by the segment of the cord into which the autonomic afferent fibres enter. Anaemia of the myocardium results in a similar sensory manifestation which we call angina pectoris. There are a number of unexplained points in this conception of referred pain, and some workers have suggested totally different and even more improbable hypotheses.

Throughout the autonomic system we find connector neurones leading to effector cells, which deliver the nervous impulses to the part supplied. Experimental evidence leads us to believe that the effector cells have conduction characteristics, seen nowhere else in the neural tissues of the body, which enable them to excite smooth muscle to activity. The effector neurones are some-

times called "transformer" cells for this reason.

In skeletal muscles, almost any degree of contraction or relaxtion can be attained through the controlling influence of a single nerve. Most of the smooth muscle of the viscera has a double control. Take the gut as an instance. The sympathetic system inhibits its activity as a whole. The parasympathetic system is capable of selectively activating any part of the gut. Thus, by the interaction of the two systems, any degree of separate activity can be attained. There are certain exceptions to the general rule in the actions of these systems, and we will treat these later.

Cranial Division — Parasympathetic System.

The function of the reflex pathways, included in this system, may be described as protective, constructional and conservative. By reflex narrowing of the pupil of the eye protection against excessive retinal illumination is attained. The induction of salivary and gastric secretions and the activation of the upper alimentary tract, with periodic inhibition of the sphincters, ensures adequate digestive processes, which are the first step in the metabolic or constructional activities of the body. The slowing effect on the heart rate is a conservative action, and is of major importance in the control of the blood pressure. This control is probably actuated by afferent impulses from the region of the carotid sinus, acting through the vagus nerve to produce a decreased impulse formation, conduction time and contraction of the heart muscle.

Sacral Division — Parasympathetic System.

The reflexes of this division are chiefly concerned with the evacuation of certain hollow viscera. Evacuation is produced by the contraction of the muscular walls of the viscus with a concomitant relaxation of the sphincters. The distal colon, rectum, urinary bladder and seminal vesicles are controlled in this manner. The reflex is set up by the distention of the hollow viscus, and is, in every case, under voluntary control to a large measure. Certain pschyic impulses can cause involuntary evacuation, due possibly to sympathetic impulses activating the sacral parasympathetic system at their juncture in the pelvic plexus.

Sympathetic System.

The actions of this system are always diffuse, due to the extensive interconnection between the neurones of the lateral sympathetic trunk. Each connector fibre has outlet into several effector cells. This is quite unlike the mechanisms which we have just ennumerated in connection with the parasympathetic system, where each reflex arc is quite circumscribed in its field of action.

The function of this system seems to be mainly adaptative. It tends to prevent the external environment upsetting the internal environment, which consists chiefly of the body fluids, to a point incompatible with effective activity. The results of sympathetic stimulation are seen in their grossest forms when set in motion by fear or rage. The sympathetic system may be considered the instrument of man's urge towards self-preservation.

Sympathetic stimulation dilates the pupil of the eye, retracts the upper eyelid, and pushes the eye-ball forward in the socket. The sweat glands are stirred to violent activity, the hairs of the body stand up, and the small blood vessels of the skin are constricted. Vessels of the splanchnic area are also constricted, and with the increased heart rate we get a rise in blood pressure. These effects tend to send an increased flow of blood through the brain, heart and skeletal muscles. There may be an added dilatation of the coronary vessels, which would further increase the flow through the heart. The number of cellular elements in the circulating blood is considerably increased by an active contraction of the spleen. Dila-

tation of the bronchi facilitates aeration of the blood.

All muscular and glandular activity of the alimentary tract is inhibited and the sphincters are tightly closed. Inhibition of the bladder musculature with activation of the sphincters in the urinary and generative tracts is also seen. All the activations and inhibitions resulting from sympathetic stimulation may occur to almost any degree, but always tend to be diffuse.

The thyroid and adrenal glands pour their secretions into the blood stream in added quantities under the influence of sympathetic activity. The former probably raises the metabolic rate and mental acuity of the individual, whereas the latter, adrenalin, simulates sympathetic stimulation throughout the body. Some workers claim that the phenomena attributed to the sympathetic are only brought out fully in the presence of adrenalin. It would certainly seem that adrenalin prolongs the various processes that have been initiated by the sympathetic system. Adrenalin has the added power of shortening the clotting time of blood, hence effecting earlier repair of an injury. It also mobilizes liver glycogen, and thus combats the incipient hypoglycæmia due to increased muscular activity.

Complete removal of the sympathetic control has been effected experimentally in animals. Under sheltered laboratory conditions, the animals live an apparently normal life. However, their ability to do work is greatly decreased; they may show hypoglycæmic shock when exercised, and they are unable to keep a constant body temperature in the face of extreme external temperatures. Reactions to psychic stimuli are defective from the physical standpoint.

Pharmacology.

Adrenalin is the most important drug acting on the autonomic nervous system. Its site of action is the myoneural substance, which is the hypothetical intermediary between the effector fibre ending and the muscle substance. The action of this drug is excitatory, and, as previously described, almost exactly simulates sympathetic stimulation. Tyramine acts similarly. Ergotoxine and ergotamine first excite and then paralyze all the motor sympathetic endings.

Pilocarpine stimulates all the parasympathetic nerve endings. Physostigmine apparently does the same thing, although there are some indications that this drug merely facilitates the passage of impulses already present. Thus, physostigmine probably has no stimulating action, but renders effective impulses which would otherwise never have reached the terminal organ. For this reason it is a perfect antagonist of atropine and hyoscine, both of which paralyze parasympathetic nerve endings.

Acetyl-choline stimulates all the parasympathetic nerve endings. Experimentally it has been shown that, when a parasympathetic nerve is stimulated, acetyl-choline is liberated at the terminal organ. This is most easily demonstrated at the vagus endings on the heart, and acetyl-choline has been called the "vagus substance." The action of artificially applied acetyl-choline is almost as transitory as the effect of a nerve impulse, and so it is not unreasonable to suggest that this is the effector substance of the parasympathetic system.

The action of nicotine on the autonomic system, sympathetic or parasympathetic, is quite unique. Applied directly to ganglia, it first stimulates and then paralyzes the junction between connector fibres and effector cells. This drug has been widely used in tracing the tracts of the autonomic nervous system.

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Some Aspects of Bronchial Asthma.

By ROBERT DAWSON RUDOLF, M.D. (Edin.).
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Hay fever and asthma are often described as manifestations of the same condition, but although they are frequently associated, they are, in my experience, usually separate. A person may suffer from paroxysms of sneezing, running at the nose and conjunctival congestion for years and never have any respiratory distress; and, on the other hand, most cases of bronchial asthma are free from these signs of upper respiratory congestion. The therapy of the two conditions throws light on the difference between them, for while the hypodermic use of adrenalin will usually quickly relieve true asthma, it has little effect on hay fever, unless, indeed, it be applied locally.

It is with true bronchial asthma that these scattered remarks are concerned.

What is the nature of the condition? The symptoms undoubtedly point to some obstruction in the smaller bronchi, which leads presently to distension of the lungs. In his struggle for breath the patient takes short inspirations, followed by long wheezy expirations as he endeavours to overcome the resistance to the output of air. The reason why the difficulty is chiefly expiratory is probably because the muscles of expiration are weaker than those of inspiration. Soon there is added the loss of elasticity of the lungs, which in normal quiet respiration is the chief factor in expressing the air from the chest. Professor W. E. Dixon(14) has shown experimentally "that the greater the distension of the lungs the less the elastic recoil when the distending force is removed." The chest will presently be in a position of full inspiration, and X-ray examination shows that the diaphragm is flat and immovable, it being no longer drawn up during expiration by the elasticity of the lungs.

The immediate cause of the bronchiolar narrowing has for long been a subject of much discussion, and even yet all are not agreed, although most consider that it is due to spasm of the bronchial muscle. (By the way, the wheezing is often low-pitched, which would suggest obstruction of the large tubes as well, but this point never seems to be dwelt upon).

To take the spasm theory first.—The muscular coat of the bronchi is best developed in the smaller tubes. The nervous motor control of this coat is through the vagus, and there is much experimental evidence that stimulation of that nerve produces contraction of the bronchioles. Both direct and reflex stimulation give this result and Brodie and Dixon found that the reflex from the nose was the most active here, and this has been confirmed by many other workers. The inhibitory nerves are the sympathetic. Now it is well known that atropine paralyses the vagal nerve endings, and it often relieves the spasm of asthma. Also, adrenalin stimulates the sympathetic neuro-muscular junctions and hence should inhibit the spasm, and adrenalin is one of our best remedies in asthma. Thus both experimental and clinical evidence seem conclusive that asthma is due to spasm of the bronchial muscle, whatever may cause that spasm.

There are, however, several difficulties in the way of accepting this bronchial spasm as fully explaining asthma. Associated with a paroxysm there is usually some increase in bronchial secretion, and the sputum often contains Curschmann's spirals, Charcot-Leyden crystals and eosinophile cells. This picture is suggestive of engorgement of the mucous membrane and it is difficult to see how mere contraction of the muscular coat could produce it. In guinea pigs suffering from anaphylactic shock there is usually much asthma and the bronchial mucous membrane is found to be enor-

mously engorged and oedematous. By the way, it should be noted that guinea pigs are the only animals in whom experimentally - produced anaphylaxis causes asthma, so one cannot rely too much on such evidence in the case of man.

When a person has hay fever the nasal mucous membrane can be seen to be in a state of congestion, and when the condition is complicated with asthma it is reasonable to assume that the same engorgement is occurring further down. Indeed, P. Vallery-Radot(8) in speaking of paroxysmal coryza occurring apart from pollen sensitivity would call these cases "nasal asthma." The coarse wheezing that so commonly is present in asthma would suggest congestion rather than spasm of the larger tubes, as these have little power of contracting.

No one holds for a moment that the condition is an inflammatory one, but rather a vaso-neurosis, as occurs in urticaria and certain erythematous drug rashes.

It seems probable that both theories are right and that in some cases of asthma bronchial spasm predominates and in other mucous engorgement, but probably some of each factor is usually present in every case. In support of this common double causation are the findings of Huber and Koessler(2), who noted great thickening of the bronchial mucous membrane and also hypertrophy of the smooth muscle of the bronchiolar walls in six persons who had died of anaphylactic asthma. Moreover, X-ray examinations usually reveal tissue changes in the bronchi, which are suggestive of more than mere spasm.

When one comes to the actual causes of asthma, be the bronchial narrowing due to either spasm or mucous engorgement, or both, such a variety of factors present themselves that chaos seems to reign, but the matter may be simplified if we look on all these causes as acting in one of two ways,—either by increasing the irritability of the neuro-muscular apparatus of the bronchi, or by acting as afferent stimuli of this mechanism.

The first factor seems the more important. The sensitivity is so slight in most people that almost any amount of afferent impulses fail to produce the bronchial narrowing. Occasionally, however, if the irritation be strong enough this may occur, as in the case of a woman of middle age who had never suffered from asthma but who, following the inhalation of a tooth during extraction had typical attacks which only cleared up when she had coughed out the foreign body. In some, on the other hand, the sensitivity is so great that attacks seem to occur almost spontaneously or at any rate from very slight afferent causes. As Goodhart and Spriggs(3) put it, "Given a certain sensitiveness of the nerve centres, anything seems capable of producing an attack. It may be a nervous shock, anger or other emotion, over-fatigue of mind or body, too monotonous a habit of living, too little exercise, too much food, indiscretions in the nature of the diet, constipation, uterine disorders, changes of temperature, changes of climate, a thunder-storm—changes in the weather seem to be particularly prone to induce asthma—microscopic organisms in the atmosphere, such as the pollen of hay, or dust and fluff, or emanations of various kinds from animals (cat and horse asthma) and so on." It is easy to realize on reading such a list that most of the factors mentioned act by increasing the sensitivity of the mechanism although some increase the afferent impulses and thus act reflexly.

It must be remembered that the muscular coat of the bronchi is constantly in a state of semi-contraction which varies the whole time, being greater during expiration and relaxing during inspiration. In asthma the contraction is exaggerated, a cramp as distinguished from a mild contraction. The vascular tone is also subject to constant variations and vaso-dilation will cause bronchial narrowing.

The physician usually first sees a case of asthma during a paroxysm and

when this is over it is very necessary for him to go thoroughly into the history in his endeavour to find the special *bete noire* which for this patient is the precipitating cause.

An underlying nervous instability is, with rare exceptions as already mentioned, a *sine qua non;* and this may be inherited directly as asthma, or a family instability may be shown by the occurrence of migraine, epilepsy, urticaria, etc. Given some such instability, various factors may increase it, such as nerve strain, toxaemias, etc. Some would have us believe that this hypersensitiveness is always due to some toxaemia, but with this I cannot agree. Climatic conditions frequently seem to influence it, and often a thunder-storm will precipitate an attack as it does one of epilepsy. It is unfortunate that we know so little of how climate affects people. At present much investigation is going on in regard to this, largely in Germany(10), but so far with little definite result. Climatic treatment is still largely empirical although none the less important on that account.

Having investigated all possible causes of nervous instability it is necessary to look for any sources of afferent impulses, which may be the final cause of throwing the sensitive mechanism into a storm. Such impulses may come from diverse parts of the body. For example, many only have asthma during a spell of bronchitis. Asthma of this nature is often termed "bronchitic asthma" as distinguished from bronchial asthma. Irritation in the upper air passages, especially the nose (and chiefly the posterior portion of the septum), the sinuses, the teeth and the ears may be mentioned. Uterine asthma is often spoken of, but I have never come across a case of it. An indigestible meal is often a cause. This may act reflexly, but probably often produces toxins which enhance the nervous irritability. Marvellous idiosyncrasies are found with regard to the reflex production. I know a man who only gets an attack when he goes out on a keen frosty day, and this no matter how carefully he muffles his nose and mouth. Graves tells of having in one day come across two cases of asthma, one of whom always had an attack when the chimney smoked and the other was never so free from it as under these conditions. Everyone has met with these peculiar idiosyncracies.

Many patients find that they are free from attacks in certain localities and yet suffer in others although their mode of life is in every other respect the same. I recall a man who lived in Montreal till after middle life without having any asthma, and yet when he moved to Toronto (and he has tried several parts of this city) he is a martyr. If he returns to Montreal he is again free. I have no doubt that instances might be produced where the opposite was the case. I knew a mother and daughter in England who were both victims of asthma. They searched Europe for a climate that would suit them both, but if one was well the other suffered, and at last they compromised on the large, smoky, manufacturing town of Birmingham, where they were both fairly comfortable.

Every clinician knows how difficult it is to demonstrate a paroxysm of asthma to his class, the mere bringing of the patient into hospital being usually sufficient to stop the attacks. Fowler and Godlee(4) speak of "Saturday and Sunday asthma" as being common at the Brompton Hospital Outdoor Clinic. "The state of the nervous system in these people is so sensitive to the slightest change in the routine of life, such as occurs at the week-end, that they may then have attacks although free from them during the rest of the week."

If allergy, or hypersensitiveness to certain extraneous substances be suspected, and this is specially likely in asthma commencing early in life, the various skin tests should be tried and an attempt made to produce immunity to any inculpated substance by innoculation. Once the specific allergen is recognized (and this is often clear from the history), the patient must avoid

contact with it as far as possible. Who has not seen asthma escaped from by the avoidage of feather pillows or the vicinity of horses and stables? In my opinion, however, allergy only explains a fraction of the cases. J. S. McLaughlin(5) found in 23,725 skin tests done on 1,281 cases of bronchial asthma that 2,780, or 11.5 per cent., were positive. I think that most will now agree with the editorial writer in the Journal of the American Medical Association who wrote in 1929: "Detectable allergy at best accounts for only a fraction of the cases of asthma that come under observation."(11).

Focal infections are often blamed for the production of asthma. No doubt they occasionally act, by inducing a toxaemia, by reflex disturbance or by lowering the general health, but such are not a common cause of the condition, and I note that Rackemann and Tobey(12), a couple of years ago in a statistical study of The Nose and Throat in Asthma, carried on at the Massachusetts General Hospital in Boston, came to the conclusion that "local treatment of the nose, throat and teeth had apparently brought about permanent relief in about five per cent. of the cases." Operations on the nasal passages for the relief of some physical abnormality often temporarily relieve asthma. My limited experience, however, would agree with that of Clendening(6), who is not impressed with the results as regards permanent relief. He quotes Kahn's review of a series of cases followed for some time after operation. "No cures of the pre-existing asthma followed nasal surgery," and also Lintz, who has come to the conclusion that "intra-nasal operation as a cure for bronchial asthma is futile." I have asked my colleague, Professor Perry Goldsmith, who has charge of the Nose and Throat Department of the Toronto General Hospital, what his experience has been in this regard, and he writes as follows: "When surgery is indicated in sinus infection, and has been efficiently carried out, very marked improvement in the local symptoms in the nose follows. Recurring head colds are largely prevented, nasal and postnasal discharge greatly lessened, and the upper respiratory mucous membrane is in a much less irritable condition. The effect on asthma, however, has been very disappointing. It is true some very dramatic improvements have immediately followed operation, but the benefit has in most instances been only temporary."

It by no means follows that any obvious abnormality in the upper air passages should not be treated in every approved manner, but hopes of permanent relief of asthma from such proceedings are slim. To quote B. Haseltine(13): "Nasal irritation alone cannot cause bronchospasm."

In many cases a change in environment or the removal of some cause of hypersensitivity or of increased afferent impulses may be followed by dramatic cessation of the attacks, but it must be admitted that permanent success is not as common as we would desire.

There are, however, several drugs which will often keep the patient fairly free from attacks as long as they are being taken, and may even occasionally lead to apparent cure. We cannot sometimes say exactly how they act, although no doubt it is chiefly by decreasing sensitivity. Such are the iodides, the bromides, arsenic and belladonna.

I have known many patients to remain practically free from paroxysms while taking such a mixture as the following:

R/
Potass. Iodid.....dr. 1
Potass. Bromid.....dr. 3
Liq. Arsenical.....min. 60
Tinct. Belladonn.....dr. 2
Syrup. Tolu.....oz. 1
Aq. Chloroform.....ad oz. 6
Misce.

Sig. A dessertspoonful in water twice or thrice daily after meals.

"Protein shock" seems to have a profound influence in lessening nervous hypersensitivity, and the intravenous

injection of 2.5—3 cc. of a five per cent. solution of peptone is often followed by great lessening of the attacks. The best peptone to use is probably Armour's No. 2(7). It is likely that many vaccines and other methods, such as the injection of the patient's own blood, act in this non-specific way not only in asthma, but in many conditions.

Frequent asthmatics may ward off an impending attack by inhaling the fumes of some burning powder or cigarette. There are many of these on the market under proprietary names. They all resemble more or less the *Pulvis Lobeliae Compositus*, which contains potassium nitrate, lobelia, stramonium and black tea. Sprays are also commonly used for the same purpose, such as Tucker's, in which are atropine, cocaine and sodium nitrite. The risk of the cocaine habit being formed is evident.

It is in the warding off of impending attacks that ephedrine is so useful, and it is not nearly as effectual as adrenalin during the paroxysm. A great advantage is that it acts well when taken by the mouth. 50 mg. at bedtime is an ordinary dose. An objection often raised by patients is that although it averts the attack it causes nervousness and thumping of the heart, which interferes with sleep. This common adverse effect can be avoided by combining a grain of luminal with the dose.

I will not burden these disjointed remarks with a list of cases, but would like to mention two where ephedrine was of much service.

Case 1.—A woman of 40 came suffering from terribly severe and constant asthma of long duration. Every sort of examination failed to reveal any organic or allergic cause, and she was only kept going in hospital by frequent hypodermic injections of adrenalin, often requiring as many as twenty of these daily. Then she was given 50 mg. of ephedrine sulphate night and morning *per os*, and soon the adrenalin became less required and then unnecessary. She continued this for some time after returning home, then only at bedtime, and finally only occasionally when she feared an attack, and when last seen a year later was free of asthma.

Case 2.—A woman of 50 had suffered from severe asthma for over ten years. Her home was in Eastern Canada, and her doctor, after trying many methods of treatment, sent her to the Western prairies, but she obtained no relief and came to Toronto, where I sent her into the hospital for thorough examination. There was much emphysema, and the chest was full of accompaniments. The X-ray report read: "At some previous time a mimimal degree of tuberculosis of the lungs, but healing has taken place, and there is no evidence of active condition." The blood pressure averaged 140|75. She improved considerably under a mixture like the one mentioned above, and returned home, but months later the asthma came back in spite of the medicine. Then she was given in addition 50 mg. of ephedrine sulphate at bedtime, and later reported that this always averted the attacks, but caused excitement and insomnia. When one grain of luminal was added, the result was excellent, and a report a year later stated that she remained free from attacks but occasionally took the ephedrine and luminal.

No attempt has been made here to discuss the treatment of bronchial

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asthma in detail. Rather I have tried to bring into prominence the underlying principles of the causation and therapy of this very distressing condition.

Professor D. P. D. Wilkie, of Edinburgh, in opening a discussion of the surgical treatment of septicaemia before the British Medical Association last summer, made the following very philosophical remark, which I would venture to apply to the treatment of this most elusive disease, asthma:—"We are so apt to enthrone in the sunshine of our memory the apparently striking success and to allow the many failures to slip into the quiet shadows of forgetfulness."

Summary:

1. Asthma is due to bronchiolar narrowing, which may be caused by muscular spasm or mucosa engorgement, or both.
2. In nearly every case two factors exist: (a) a hypersensitivity of the nervous mechanism; (b) increased afferent impulses from some part of the body.
3. In the treatment, search should be made for any possible causes of this hypersensitivity and for any sources of reflex disturbance, and these, if possible, removed.
4. Often drugs will lessen the sensitiveness of the mechanism and the strength of the afferent impulses, and may in this way produce symptomatic relief.

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Primary Peritonitis.

By M. W. SELZNICK, 32.

Definition.

By primary peritonitis is meant that form of infection with the pneumococcus or streptococcus in which the peritoneal symptoms are the predominating feature of the illness. It is fairly reasonable to suppose that the peritoneal lesion is nearly always secondary to some other focus in the body, but when that focus is latent or of minor importance it is customary to use the above term.

Blood-infection without any ascertainable focus of origin does occur, but more frequently infection spreads from the Fallopian tube, or possibly from the intestine. The disease is much more common in females under the age of ten, but may occur in males of the same age period.

Etiology.

In a large number of cases, at operation or autopsy no other lesion than the peritonitis has been found, the infection apparently being primary in the peritoneum. These cases are usually spoken of as primary. In a smaller group, less than one-third of the cases, there has been an antecedent pneumococcal or streptococcal infection of the lungs, pleura, or middle ear, and such cases are spoken of as secondary.

In a still smaller group, the infection of other organs and the peritoneum are apparently simultaneous, and the peritonitis seems to be part of a general infection. Blood cultures in these are positive, at least in the early stage in a large number of all cases.

Mode of Infection.

In regard to the way in which the infection reaches the peritoneum, in the latter generalized group it is probably through the blood stream, and in the secondary cases which follow an antecedent pneumococcus or streptococcus infection, such as was formerly supposed, through the intestinal wall, inasmuch as diarrhea is a common symptom. On the other hand it is practically proved that in most, if not in all primary cases in females the infection enters by way of the Fallopion tubes. About 75% of all cases of pneumococcus peritonitis occur in little girls under ten years of age, with as many under five as after. The cases occurring in boys and in adults seem all to be secondary or part of a generalized pneumococcus infection. In the cases of primary pneumococcus peritonitis that have been carefully observed, pneumococci of the same type have been isolated from the peritoneum, the vagina and the blood, and the peritonitis has been severer in the pelvis than in the upper abdomen. Furthermore, inoculation of the vagina in young female monkeys has produced pneumococcus peritonitis without causing symptoms till the peritoneum was involved. At operation in the early stage of the disease there is more exudate in the pelvis, and Blake (Nelson's System of Surgery) has stripped pus from the Fallopian tubes. Also, in the cases which localize in abscess, the abscess is usually in the pelvis or lower abdomen, resolution of the peritonitis having occurred above.

Considering the rarity of primary infection of the peritoneum, it is reasonable to believe that all except those forming part of a more or less overwhelming general infection are caused by the infection of an organ and the continued extension of this infection to the peritoneum. If this theory be correct, the accepted classification of these cases is wrong, and the so-called primary cases are actually secondary to pneumococcus or streptococcus infection elsewhere. The important bearing of this assumption must be thoroughly considered in treatment of this condition.

Morbid Anatomy.

The peritonitis is diffuse at the start and may continue so or become localized In the early stages there is not the tendency to the formation of adhesions observed in other forms of peritonitis. In cases of tubal origin the process is more active and advanced in the pelvic region and sometimes, as has been said by Blake, pus may be made to exude from the tubes by stripping them. The exudate is rather thick, milky or flaky pus, almost seropurulent, of a grayish-yellow or greenish color and without odor. The peritoneum is not always markedly reddened and often has a slimy slippery feel. In those cases that go on to partial resolution and abscess formation, the exudate becomes thicker, adhesions form and the abscesses thus formed are usually large and situated in the lower abdomen. If not opened, they may reach enormous size and may evacuate themselves spontaneously, usually through the umbilicus. Coexistent pneumonia, pleurisy, and pericarditis are common in the cases of general infection. In the severer cases the pneumococcus is generally found in the blood.

Course and Symptoms.

The symptoms vary considerably. They are those of peritonitis of varying grades of severity. One can with advantage describe three stages to the disease—the stage of onset, an intermediate stage, and a residual stage (Waugh).

The stage of onset starts abruptly with abdominal pain, vomiting, and fever, which may reach 104 or 105

degrees F. In some instances there is noticeable diarrhea. Frequently there are toxic symptoms out of proportion to the local findings, and delirium may be noted.

The abdominal pain may be diffuse, but is usually more definite in the hypogastrium. The abdominal wall may be rigid, but more often is soft, and there may be but slight local tenderness. In the very severe cases, which are always septicaemic for a time, death may occur within two or three days.

The intermediate stage corresponds to the formation of pus within the abdominal cavity. The toxic symptoms lessen, but irregular fever persists, and there is a gradual tumescence of the abdomen (Waugh). Leucocytosis will be observed Abdominal pain in this stage is very slight, and the continued fever and a painless tumid abdomen may cause a suspicion of tuberculosis.

The residual stage corresponds to the definite localization of pus and the absence of all acute symptoms save fever of an irregular type. The pus may be in the pelvis, in the central part of the abdomen, or even in the subphrenic region.

Diagnosis.

The diagnosis in the first stage has to be made from acute appendicitis. This is sometimes very difficult, but if the initial fever be high, if the abdominal signs are rather indefinite, and especially if there be slight delirium and troublesome diarrhea, one should suspect pneumococcal peritonitis. Where the condition occurs in young girls, some help may be obtained by examining the vaginal secretion for the pneumococcus, since Fraser has shown that the Fallopian tube is here the common rout of infection. If there is any serious doubt it is wiser to recommend exploration, since more harm is likely to result from allowing a septic appendix to perforate than from exploring an early pneumococcal peritonitis.

In the intermediate stage the continued fever, tumidity of the abdomen, and comparative absence of abdominal pain and tenderness may lead to a suspicion of tuberculosis peritonitis or even typhoid fever. The history of onset, the palpitation of any enlarged glands or masses in the abdomen, or the positive result to one of the recognized tests for tuberculosis may help to diagnose the former; whilst the absence of leucocytosis, an enlarged spleen, and a positive agglutination test would point to typhoid.

In the third or residual stage a definite swelling will be detected in some part of the abdomen; this is a residual abscess, and may be in the pelvis or upper or middle abdomen. The diagnosis in this stage has to be made from the other causes of abdominal tumour and abscess. The history of the previous illness will be of the utmost importance in deciding on a diagnosis.

It has been mentioned above that primary peritonitis may not give rise to the muscular rigidity which is usual with most other forms of acute peritonitis. Cope has known the combination of abdominal pain, vomiting, and lax abdomen to give grounds for diagnosing acute intestinal obstruction.

If there be coincident pleuritis or pericarditis the symptoms of peritonitis may be entirely overshadowed. In the early stages of a polyserositis it is often very difficult to determine the exact diagnosis, but if definite signs declare themselves in the lung it would be inadvisable to recommend opening the abdomen until there are sufficient grounds for suspecting the presence of pus. If the thoracic condition has been successfully treated, but the patient does not progress, special care must be paid to the abdomen, for the absence of rigidity and the comparatively slight pain may allow a considerable collection of pus to go unobserved. Waugh draws attention to the significent tumescence of the abdomen in these cases.

Blake says, with expectant treatment, some cases probably resolve and become chronic, with abatement of the

general symptoms and the formation of a local collection of fluid increasing in size and not having the sharp boundaries observed in the ordinary local peritonitis. It is difficult to form an opinion as to the percentage of cases that will localize under the expectant treatment, but it is interesting to note that in a total of 148 cases found in the literature of the last seven or eight years only fifteen were reported as local. However, many cases were operated on in the diffuse stage which undoubtedly would have localized under expectant treatment. The mortality in the diffuse cases is higher, in the neighborhood of 60%, whether or not operation is performed; although it varies greatly with different operators. Some report an absolute mortality and others almost uniform recoveries. The prognosis of operation for the localized cases is good, there being few deaths reported.

Summing Up of Diagnosis.

The occurrence of diffuse peritonitis in young children, particularly girls, without tenderness in the region of the appendix, should lead to a strong suspicion of pneumococcal or gonococcal peritonitis. More than usual distension, a doughy resistance, a high white count of 25 to 40,000 with marked prostration, according to some authorities, would warrant the diagnosis of pneumococcal peritonitis. The diagnosis may be verified by vaginal smears and cultures. Agglutination test with the patient's serum have given positive results as to the type of pneumococcus and should be taken, particularly if serum treatment is to be given.

Treatment.

If the diagnosis cannot be made from appendicitis, then the treatment must be the same, that is, early operation, to make sure that an acute appendicitis will not be missed. But if the correct diagnosis is made more conservative treatment seems to produce better results in early diffuse cases, as the patient is in no condition for operative interference, and the results obtained are much better if our energies are directed towards getting the patient into better condition, with increased immunity.

Fluid is the first essential, and salines and glucose should be given to replace the loss by prolonged vomiting and diarrhea. Locke's solution seems admirable for this use. About 35 cc. per pound of body weight in 24 hours should be our guide for the amount administered. The fluid supplies the tissues with water, the saline restores the chloride balance, the glucose overcomes the acidosis, and all three act as natural stimulants to the kidneys in removing the toxic products of the disease.

Transfusion of whole blood has been used and is very good for supplying fluid and for stimulation.

The administration of anti-pneumococcic and anti-streptococcic sera is recommended. Over 50% of the pneumococcic cases are type 1, and also the serum should be used at once pending the typing. Connaught laboratories are now producing a serum for both types 1 and 2. Polyvalent anti-streptococcic sera are also given, but results with this treatment are vague.

When the condition has been localized, with the help of constant applications of heat to the abdomen in any form, but especially by poultices and electric cradles, then the best procedure is to drain the localized abscess.

Case Report.

(This is a history of a case described by Dr. John A. Duncan of Sault Ste. Marie, Ontario, and formerly of the staff of the Hospital for Sick Children, in the June, 1931, number of the Canadian Medical Journal).

A little girl, seven years old, was taken ill in December with vomiting, abdominal pain and gradually increasing diarrhea. When the doctor was called two days later, the child described the pain as being all over the abdomen, and complained also of pain on voiding urine. She seemed in great pain, her lips were dry, her tempera-

ture was 104 and pulse 148. Her mouth, nose and throat, heart and lungs were normal. The abdomen was not distended or rigid, but there was a generalized tenderness, especially acute in the lower quadrants. Rectal examination brought out tenderness, but no pelvic mass. It was noted, however, that the opposing surfaces of the labia were inflamed and moistened by a serous discharge. The urine was normal, white blood count was 27,000, mostly polymorphs. Provisional diagnosis was primary peritonitis. This was confirmed by finding gram positive diplococci from abdominal paracentesis.

There was apparently some controversy as to the true condition, and an exploratory laparotomy was done, and odorless, thin pus with flakes of fibrin was found, and the intestines exposed were red and loosely adherent to one another with fibrinous exudate. The appendix was involved, not more than the rest of the viscera, but it was removed. A drain was put in the bottom of the pouch of Douglas and another in the right iliac fossa, without further exploration. The patient was then given 1000 cc's of normal saline interstitially and returned to bed in good condition.

A pure culture of pneumococcus of undetermined type was obtained from the abdominal exudate. That night her temperature went up to 106. Continuous intravenous of Locke's solution was started and she received the first of several therapeutic doses of anti-pneumococcic serum, type 1. (Connaught Lab.). By the fourth day her temperature was 103 degrees and her white count 15,000. At the end of a week her temperature was rising again and suspicions of a left-sided empyema were confirmed by aspiration. A pure growth of pneumococcus was obtained from this Her general condition, however, was encouraging and for the next two weeks she was relieved by the removal of 100 to 150 cc's of thin, seropurulent pus every second or third day.

At this time it was noticed by the nurse that the vaginal discharge had become more profuse and purulent. The patient continued to complain of diarrhea and abdominal pain and soon a large mass could be definitely felt in the left lower quadrant. This was not interfered with till four weeks from the onset of the illness, when a pint of greenish pus was obtained by a left rectus incision. A large drain was inserted and at the same time the empyema was drained by a rib resection. Further recovery was without incident and in two weeks she went home. In three months she was in excellent health.

General Complications.

Duncan reports the commonest complication of primary peritonitis to be empyema. This occurred thirteen times in the pneumococcic group and nine times in the streptococcic. Lobar pneumonia occurred in fifteen per cent. of his cases and broncho-pneumonia in ten per cent. of the streptococcic cases, three of whom were males. All those with pneumonia but one died. Septicaemia is another complication. In thirty-five of the cases described by Duncan there were seventeen septicaemias. In these the death-rate was 88%.

Duncan reports sixty-six cases from the Hospital for Sick Children, of whom one-half were due to pneumonia and the rest to steptococcus. The general mortality for the sixty-six cases was 68.6%. 80% of the sixty-seven cases were in females All but three of the pneumococcic cases were in females. Other investigators report no males in their record.

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The Carotid Sinus.

By R. C. PARTRIDGE, M.A., Department of Physiology.

The carotid sinus is a specially innervated part of the vessels and tissue which lies at the bifurcation of the carotid artery near the level of the thyroid cartilage. A study of the innervation has shown that the region is surrounded by a very rich nerve plexus whose fibres unite to form several nerves. Of these the twig which joins the glossopharyngeal is the most prominent and is usually called the sinus nerve. Other fibres join the vagus ganglion and superior cervical ganglion. Although the nerve connections in the higher animals are very complicated and vary from one preparation to another, the three main divisions are always present. The terminations of the sinus nerve are concentrated on the bulbous expansion of the internal branch of the artery with the sensitive ramification lying between the collagenous fibres of the adventitious coat. This anatomical disposition allows us to understand how the hydrostatic pressure may excite the endings by their compression between the collagenous fibres. In the bifurcation of the carotid artery the intercarotid body is found. This network of blood vessels, cells and nervous elements also sends fibres to the sinus nerve and is usually considered as part of the carotid sinus.

The region of the bifurcation of the artery through its nerve connections brings about alterations in the rate of the heart and in vasomotor tone and tends to regulate the blood pressure in the head. The present knowledge of this function of the carotid sinus has been obtained from experiments carried out within the last eight years. Before 1923, there was no logical explanation for the isolated facts that had been discovered. The workers at that time recognized that a decrease of pressure in the region of the bifurcation of the carotid artery resulted in an acceleration of the heart and general arterial hypertension, and that hypertension in this region released a bradycardia and general arterial hypotension, but they did not understand the mechanism of operation.

Hering in 1923 made a very real contribution to the solution of this problem. He proved that mechanical or electrical stimulation of this region, which he called "the carotid sinus," or stimulation of the sinus nerve involved a reflex that produced bradycardia and hypotension. He varied the pressure in the sinus region and showed that the compensatory effects did not occur if the nerve pathways were interrupted. He concluded that a changed pressure in the sinus and head region caused compensatory cardiovascular changes which were entirely reflex.

The mechanism by which the carotid sinus performs its function was clearly demonstrated by the perfusion experiments of Heymans and his co-workers. These investigators succeeded in isolating the circulation of the sinus region from the body while maintaining an intact innervation. By perfusing the isolated sinus with fluid from a Dale-Schuster pump or with blood from a second animal the control exercised by the region could be accurately estimated, since the stimulation of the carotid sinus by appropriate pressure changes was transmitted to the trunk through the sinus nerve connections and was uncomplicated by other factors. These perfusion experiments, which are described in detail in the fourth edition of "Recent Advances in Physiology," established certain facts. They showed that sinus hypotension stimulated the sinus and vagus nerves to produce tachycardia and at the same time involved the splanchnic and other constrictor nerves to change the calibre of the blood vessels in the splanchnic, peripheral and cephalic areas and to increase the adrenalin secretion so that

the vessels in the reservoir areas were constricted and the blood pressure was increased. Hypertension in the sinus region involved the same nerves to produce bradycardia and dilation of the blood vessels with the purpose of decreasing the blood pressure to nullify the hypertension in the carotid artery.

A reflex similar to that of carotid sinus origin is initiated by pressure increase in the arch of the aorta and acts through the depressor nerve to lower the blood pressure and slow the heart and thus to protect it from extremes of pressure. Since these two areas were known to exert a reflex control of blood pressure, the question naturally arose as to whether or not other arteries were provided with a similar mechanism. The question was soon answered in the negative, for after denervation of the two regions of the carotid artery there was very little compensatory blood pressure change. It has been suggested that a third area of control may exist in the thoracic region of the aorta, but the area has not been localized.

It has been established that hydrostatic pressure within the carotid artery acts reflexly through the carotid sinus and aortic zones to control the heart rate and calibre of the vessels in the reservoir areas so that a constant blood pressure is maintained in the head and in the trunk. In addition to this function which the carotid sinus shares with the aorta, is its particular function of maintaining a constant blood pressure in the head during pressure changes attendant upon changes of posture. As the nerves involved in the reflex cardiovascular regulation are of pre-eminent importance the afferent impulses which they transmit are worthy of particular attention in any attempt to elucidate the function of the carotid sinus. Since this aspect of the problem had not been investigated, a study of the afferent impulses in the sinus nerve was initiated some time ago in the physiological laboratory of this University.

The recording of these impulses has been made possible by the discovery of the radio amplifier and by its application to physiological problems The electrical change accompanying each impulse may be intercepted, amplified and recorded in a manner which leaves no doubt as to the significance of the electrical potential or of the accompanying impulse. In order to carry out a study of the afferent impulses, the sinus nerve was dissected and placed on silver chloride electrodes which were connected to a high gain amplifier and a recording instrument. The nerve potential of a few millionths of a volt lasting for a few thousandths of a second was amplified so that it actuated a speaker or a galvanometer. By using this device, afferent impulses in the sinus nerve were represented by sounds in the speaker or by vertical lines on a photographic paper. The studies carried out with this apparatus showed that with normal hydrostatic pressure, nerve impulses can be recorded in all except the sympathetic connections of the sinus region and that these impulses are absent during diastole but increase in frequency during ventricular systole and during closure of the aortic valves. It is probable that the impulses are produced by the pressure changes accompanying cardiac contraction, which operate to expand the arterial walls and to stimulate the nerve endings between the collagenous fibres of the adventitia. This suggestion is substantiated by the results of experiments carried out with the isolated sinus region. An expansion of the walls of the isolated sinus with a perfusion fluid stimulates the endings so that impulses are transferred up the sinus nerve. A variation of these impulses similar to that which occurs in the intact animal may be reproduced by suitable changes of the perfusion pressure, the impulse variation being coincident with the change of perfusion pressure and independent of the heart rate. This experiment demonstrates that the impulse character depends upon pressure

changes within the sinus region and is independent of other cardiac effects.

This intermittent impulse which is present in the sinus nerve during normal pressure within the carotid sinus region may have a physiological significance. Heymans suggests that normal impulses from the carotid sinus affect the centres so that normal tone is maintained in the cardiac and vascular nerves. In this way, it is believed cardiac rhythm and arterial pressure remain at normal levels. While the fact that removal of these impulses by section of the nerves in some cases produces hypertension and tachycardia and makes it seem as though the carotid sinus control is a fairly important factor in the maintenance of normal conditions, it is well known that these phenomena may follow any operative procedure. The contention that normal cardiac and vascular tone is maintained in part by the intermittent sinus impulses is, however, strengthened by the observation that higher blood pressure level produces a more pronounced impulse while a lower level gives a less marked response.

Sinus nerve impulses may act to bring about a compensation in the general systematic pressure when abnormal conditions exist within the sinus. With hypertension in the carotid sinus, produced by adrenalin injection, the nerve impulse changes its character. The impulses which are of an intermittent nature under normal conditions become constant and occur throughout both phases of the cardiac cycle. Coincident with this change of impulse character a fall of systemic blood pressure occurs if the impulses can pass up towards the brain. It seems quite probable that the increased number of impulses accumulating in the brain with carotid sinus hypertension affect the centres so that the compensatory fall in systemic blood pressure is accomplished.

The character of the impulses in the intercarotid sinus nerve is also changed with sinus hypotension. The impulses become less prominent as the pressure falls and are absent at low pressures. Coincident with this absence of impulse in the intercarotid sinus nerve a rise of systemic blood pressure occurs. It may be that this compensatory increase of blood pressure is brought about as a consequence of the cessation of the depressor impulses in the sinus nerve, or it may be that the sympathetic connections of the sinus region are involved particularly during low pressures in the sinus region. Impulses indicating such a function could not be recorded, but this was not unexpected, since an extensive literature review has not revealed an example of the recording of impulses in the sympathetic nervous system. Certain indirect experiments tend to favour the view that the thoracic autonomic connections may be important with low sinus pressures. After section of the depressor nerves, a reduction of sinus pressure by occlusion of the common carotids produces a hypertension which may be registered from the femoral artery and which is diminished to some extent by section of the sympathetic connections of the sinus region. The experiment indicates that the pressor effect is supplied in part at least by the sympathetic sinus connections.

The presence of impulses in the sinus parasympathetic nerve connections during normal conditions, their increased frequency with carotid sinus hypertension and their decreased frequency with hypotension indicate that these nerves have a physiological significance in maintaining normal cardiovascular conditions and in compensating for abnormal blood pressure in the carotid artery.

An extensive study of the clinical and physiological aspects of this problem will in time determine whether or not it is justifiable to attribute certain pathological states to abnormal carotid sinus function. Many workers in France and Germany are attaching a clinical significance to functional changes of the carotid sinus, but these investigators may have allowed theore-

tical considerations to influence their conclusions. They suggest that since low sinus pressure is known reflexly to produce tachycardia, hypersecretion of adrenalin and hypertension in experimental animals, these pathological states in man in some cases may be attributed to an insensitive carotid sinus. This defect in the carotid sinus response, in addition, may, in their opinion, account for cerebral haemorrhage since an insensitive sinus could not act to nullify the hypertension which it had produced and the pressure of the blood going to the head might become excessive. This defect in carotid sinus function which may be produced by sclerosis of the region, would augment the systemic blood pressure and adrenalin secretion. This reasoning would suggest that sinus hypotension may be concerned in the production of tachycardia, hypertension, cerebral haemorrhage and arteriosclerosis. Carotid sinus hypertension, on the other hand, may have a clinical importance. Hering claims that mechanical increase of pressure with manipulation of the region may account for the sudden inhibition of the heart during thyroid operations. He suggests cocainization of the sensitive area as a method of reducing the reflex cardiac effects during operations in the neck regions. These theoretical considerations were substantiated to some extent by the results of experiments with animals. Hering, Heymans, Danielopolu, Regniers, Koch, Mies, Nordmann, Flesch and others who are interested in this aspect of the problem, claim that section of the nerves of the carotid artery in experimental animals usually leads to cardiovascular disturbances. Paroxysmal tachycardia, extra systoles, ventricular fibrillation, dilated heart, hypertension, sclerosed arteries, veins and histological changes in the suprarenals (a very formidable list!) have been stated to follow denervation of the carotid artery. These investigators claim that certain clinical observations tend to support the theory that abnormal carotid sinus function leads to cardiovascular disturbances. Lack of carotid sinus control is seen in arteriosclerosis involving this region. In this case, the reflex slowing of the radial pulse which normally occurs with digital pressure on the region of the bifurcation of the carotid artery is absent or decreased. In fact, this so-called "Carotid Pressure Test" has been used in the diagnosis of arteriosclerosis and of certain heart lesions. An increase of the carotid sinus pressure by digital pressure exerted on the region has been found to relieve crisis of tachycardia presumably produced or aggravated by sinus hypothension.

Theoretical considerations, certain experiments carried out with animals, and a few clinical observations have suggested that abnormal carotid sinus response may play some part in the production of cardiovascular disturbances. The physiological and clinical aspects of this problem are being studied in an effort to determine the importance of this mechanism among those which operate to maintain a normal blood pressure and heart rate.

ATTENTION.

Announcement is hereby made of the imminent approach of Daffydil, the performances to take place on the evenings of March 17th and 18th. The committee has already been working hard and long in a praiseworthy attempt to equal or even better the excellent performances of former years, and have introduced a few precedentary offerings which must be seen to be appreciated.

The student support is even more sought after than usual, for the Faculty, having washed their hands of the show (in the matter of censorship) have warned the committee to wash the skits (pun!), and the cleanliness and Godliness of the show rests with the aforementioned committee, whose names can be obtained on request at the "Thunderer" press room.

Once again we warn you: Do not forget—March the 17th and 18th in Hart House Theatre.

Ventricular Fibrillation.

PAUL HAMILTON, B. and M., '35.

The subject matter of the following paragraphs is a review, of necessity brief, and of rather limited scope, of the work which has been done in elucidating the nature of ventricular fibrillation and the very closely allied forms of auricular flutter and fibrillation.

The Historical Background of the Subject.

The first work recorded is that of Ludwig and Hoffa in 1850, and it is to be doubted whether a better naked eye observation has been recorded since. They found that the normal beat of the ventricle was abolished when a strong direct or induced current was applied to the chamber. The ventricle first shrinks, gives a few rapid movements of small amplitude and then swells till it can no longer expel its contents. When thus ballooned the ventricles are convulsed with minute quiverings and the arterial pressure falls to zero, while over the surface, the muscle moves tremulously and contraction waves are seen to pass along the muscle fibres for a short distance. They further observed that while one area was in the state of contraction, adjacent areas were relaxed.

MacWilliam's experiments in 1887 and in the years following showed that fibrillation resulted from a change in the heart muscle itself and not as Kronecker thought from interference with a co-ordinating centre. He further showed that in fibrillation the rate of impulse conduction was lessened, and the period of absolute refractoriness was shortened. Porter, in 1894, demonstrated that ligation of the coronary arteries caused death, due to cessation of the heart beat, followed by fibrillation. Levy, in 1914, discovered his adrenalin-chloroform reaction: namely, that fibrillation was produced spontaneously when adrenalin was administered to animals under light chloroform anaesthesia (2% vapour), but overdosage with chloroform protected the ventricles from fibrillation. In the same year Mines in Canada, and Garrey in the United States, discovered the theory of circus movement, which was championed by Lewis and De Boer. The most recent work has been undertaken by Hooker and Wiggers in an effort to obtain a method of resuscitation from ventricular fibrillation due to electric shock.

The Mechanism by Which Fibrillation is Produced.

Mines obtained a sheet of dog's ventricle and punched a hole in it. On stimulation of this ring of muscle he obtained a contraction wave which circled about the ring for some time. Garrey quite independently performed a similar experiment. From these experiments and from the work of MacWilliam and Porter, Garrey propounded his theory of circus movement, in which he stated that impulses spread in all directions within the myocardial syncytium, but that owing to blocks within the tissue mass, the impulses were diverted now here, now there, weaving and shuttling among the fibres. And further these impulses passed over points which had been previously excited. That is, the impulses followed a circuitous route, but the circuit shifted from place to place with the shifting areas of block. A simple circuit is one which follows the same path over and over again without much deviation. Such a circuit will cause, in the auricle, a complete co-ordinated contraction for each complete circuit that is made. Lewis has shown that auricular flutter is caused by such a simple circuit, following a course about the base of the great veins. The normal rate for such a circuit is about 340 to 380 per minute in the human auricle. Lewis claims also

that auricular fibrillation is caused by such a circuit, travelling around the base of one of the great veins and following a very devious route.

Ventricular fibrillation is also caused by such a circus movement, but it is of the complex multiple circuit type which involves the whole of the ventricular mass. This circus movement is made possible by a slowing of the conduction rate, or a shortening of the refractory period of the muscle. It is obvious that if these two conditions obtain in the myocardium, a circus wave will travel slower than a normal excitation wave, and as a result, by the time the crest of the wave has passed a point, and returned, the fibres in this area will again be ready to respond. With a short refractory period the muscle will recover very much sooner and the same result will be obtained. In most circus movements both changes described occur contemporaneously.

Conditions Inducing Fibrillation.

By far the most usual procedure in producing fibrillations is the application of an electric stimulus. Bokok and Orban (1931) investigated the various forms of electric stimulus and found that high or low frequency currents alike produced fibrillation as well as alternating currents. Prévost and Battelli have found that direct current will also produce a fibrillation. Garry also produced fibrillation by a single electrical shock when timed to fall immediately after the refractory period. Hooker (1930) claims that in electric shock from high tension wires death is in many cases due to the onset of ventricular fibrillation.

Purely mechanical stimulation such as contact with a cold instrument, the application of a hot wire, the touch of a finger, or even the mechanical stimulus obtained in moving an animal from place to place when the animal is under chloroform anaesthesia will cause fibrillation. Sudden cooling of the heart, and especially local cooling of a coronary artery, will also cause fibrillation, yet MacWilliam cooled the heart in order to stop fibrillation. On the other hand sudden warming may cause fibrillation or increase the tendency to fibrillate.

Levy's work on the production of ventricular fibrillation under chloroform anaesthesia has already been mentioned. It seems that chloroform increases the excitability of the heart muscle when the anaesthesia is light, but when deep anaesthesia is produced, a depression of excitability occurs which is very effective in preventing fibrillation under many circumstances. The action of ether is the same as chloroform, but the excitatory condition is of a very transient nature. The underlying conditions producing fibrillation seem to be, according to most workers, a condition of abnormal metabolism, and Hooker believes that it is a change in the inherent fundamental metabolism of the individual fibre. Garrey emphasizes the fact that different areas must be relatively in a different metabolic state, for it is known that fibrillation will occur at any level of metabolic activity This idea seems to support the surmise of Gotch (1913) that fibrillation is due to some atomic disturbance of a protein-salt molecule with consequent changes in muscle behavior.

Chemical Factors in Fibrillation.

The possibility of developing a therapeutic method of dealing with ventricular fibrillation led Hooker to investigate the effects of various salts on the fibrillating heart. He described a method by which he obtained many spectacular recoveries. The method was as follows: A carotid cannula was inserted and fibrillation produced by electrical stimulation. When fibrillation was fully established he injected about 13 cc. per kilo of a 0.5% KCl solution in 0.9% NaCl. under a pressure of 150 mm. mercury, through the cannula. Heparin was added to this solution to prevent clotting. This potassium salt produced an inhibition and complete arrest of the fibrillation. Then followed an injection of 10 c.c. per kilo of a 0.023% $CaCl_2$ solution, after which 1 c.c. of 1:1000

adrenalin was administered, followed by a further injection of 15 c.c. per kilo of the $CaCl_2$ solution. All the solutions were fully oxygenated and heated to body temperature. Out of 21 consecutive experiments he obtained complete recovery in all but two cases, one being complete failure and the other doubtful. He also found that if fibrillation lasted more than 5 minutes asphyxial damage to the medullary centres lessened the chances of recovery materially. Intra-cardiac, intra-auricular and intra-pericardinal injection were of no avail. He also found that $NaHCO_3$ tended to produce fibrillation, and that considerable decrease in NaCl. concentration of the perfusate produced spontaneous fibrillation. And yet it has been found that if small amounts of KCl. or $CaCl_2$ are injected intravenously, a condition simulating fibrillation arises.

Wiggers confirmed Hooker's results, and further showed that intraventricular injection was efficacious if massage was employed. Hooker claimed that massage induced fibrillation and was too fraught with danger,—an idea first advanced by D'Halluin.

MacWilliam found that intravenous injection of potassium bromide or barium chloride produced spontaneous fibrillation, while strontium chloride stopped fibrillation. Rubidium chloride can replace KCl. to prevent fibrillation or control it, but much larger amounts must be used. Magnus demonstrated that perfusion of CO_2 will cause fibrillation. while neutral gases such as helium or hydrogen have no effect.

The Nervous Control of Fibrillation.

Woollard demonstrated in 1926 that the atria of the mammalian heart are innervated by both sympathetic and para-sympathetic systems, while the ventricle is innervated by the sympathetic solely. The sympathetic fibres come from the stellate ganglion. Levy's experiments indicate that the sympathetic system is a factor in producing fibrillation, for when under chloroform anaesthesia, stimulation of this ganglion produced fibrillation, but when removed, the heart was protected from fibrillation. In some cases stimulation of the accelerans nerves has caused fibrillation. Recently Brown and Samet (1913) demonstrated that the tendency of a cat heart to pass into fibrillation was much lessened when all sympathetic connections with the heart were severed.

According to Garrey, stimulation of the vagus makes the production of fibrillation more difficult, while if the ventricles are fibrillating an increase of vagal tone, in one or both nerves, may stop fibrillation or at least change its character. Cutting of both vagi may precipitate fibrillation. Hooker (1929) could not stop fibrillation, but he noted that fibrillation was readily induced during vagal inhibition.

It thus seems that vagal tone is a protecting mechanism against fibrillation. Levy claims that the protecting influence of vagal tone is abolished in deep anaesthesia due to paralysis of the vagal centres, for fibrillation occurs with the vagi cut when an animal is pithed, but only under light anaesthesia.

An old view was held by Kronecker that a co-ordinating centre is present which will protect the heart from fibrillating, and he used his puncture — inserting a needle at the upper end of the inter-ventricular sulcus—in support of this theory. But the work of Garrey and De Boer definitely proved that the phenomenon involved the whole tissue mass and was absolutely independent of any definite region in the heart musculature.

The Effect of Drugs in Fibrillation.

It has long been known that quinidine and hydro-quinidine are useful in arresting auricular fibrillation. However, Drury (1922) found that quinidine would produce spontaneous fibrillation in the cat's ventricle. Hooker concludes from his investigations that in general it has a deleterious effect on the ventricles.

Atropine which paralyses vagus endings, will cause fibrillation when intravenously injected; in chloroform anaesthesia it will produce an irregular tachycardia, but not fibrillation. Curare has the same effect, but often causes spontaneous fibrillation. Digitalis and other members of the digitalis group cause ventricular extrasytoles, and auricular fibrillation, but whether it can be held responsible for ventricular fibrillation has not been recorded. MacWilliam found that urethane and hirudin, when injected intra-venously or intra-ventricularly, will prevent fibrillation if it is not present, or will completely arrest it. Nicotine tartrate, when injected intravenously in cats under light chloroform anaesthesia, causes fibrillation, but this may be due to a liberation of adrenalin, for Dale and Laidlaw (1912) found that nicotine caused increased adenalin liberation.

Hooker investigated caffein-sodium benzoate, cardiazol, coraline, coramine and digitalin,—drugs reported to have a therapeutic cardiac action, but found that they were either without benefit or accentuated fibrillation.

Levine and Matton recorded an interesting case of Stokes - Adams syndrome followed by cardial syncope. Electrocardiographs revealed that ventricular fibrillation lasted in one attack for 3½ minutes. The injection of adrenalin chloride directly into the ventricle produced prompt recovery.

Summary.

It is generally conceeded that ventricular fibrillation is due to a circulating wave of contraction which convulses the whole mass of the ventricles. It arises from a derangement of the normal metabolic functions of the heart muscle, such that the absolute refractory period is much abreviated, while the conduction time is lessened, in some cases to nearly one-half its normal value. It can be produced by either mechanical, chemical, electrical or nervous stimulation. A method of control of fibrillation as propounded by Hooker leads to the view that the changes which cause fibrillation are of a chemical nature. Its control by the perfusion with potassium salts followed by calcium salts, has been worked out. The chief nervous mechanism which seems to control fibrillation is possibly the sympathetic control, but it also seems that vagal influence must be considered in large measure. No drugs have been found which have produced any definite change in fibrillation, which would warrant their use as a preventative or therapeutic agent. The dangers which attend light and intermittant chloroform anaesthesia have been shown, in contrast to the comparative safety from cardiae syncope due to fibrillation, under deep anaesthesia.

References.

Garrey: Phys. Revs. 1924; 4, 215.
Hooker: Amer. J. Physiol., 1929-30; 91, 305.
Levy: Brit. Med. J. 1912; 2, 502.
Wiggers: Amer. J. Physiol. 1930; 92, 223.
Lewis: Mechanism and Graphic Registration of the heart beat.

LIVER EXTRACTS IN PERNICIOUS ANAEMIA.

Since the discovery by Minot and Murphy of the beneficial effect of a high liver diet in pernicious anaemia the use of liver has been greatly extended, with a corresponding change in price. Extracts first described by Cohn of Harvard, are about twenty times as active as the original liver, depending on the yield obtained. These are not unpalatable, and when taken in soups the flavour is well masked. To a patient who must take the equivalent of a large amount of liver, such an extract is of great value.

It has been found that the mucosa of the stomach is also beneficial in pernicious anaemia. This is an exceedingly interesting finding, in view of the achlorhydria found in this disease. The preparations from this source, however, are no better than liver, and are possibly more expensive to prepare, find-

ing their chief value in alternation with liver extracts to make the diet less monotonous.

The claim of isolating the principles active in pernicious anaemia was made in 1930 by West and Howe. These were stated to be two amino-acids, beta-hydroxy glutamic acid, and gamma-hydroxy proline. These workers, however, have retracted their claim in a recent issue of the Journal of Biological Chemistry. Hence we are still in the dark as to the nature of the active principle, be it an enzyme, a hormone, or some essential amino-acid. When more active extracts are prepared, they will no doubt be available for intravenous injection. Already extracts of liver have been made with sufficient purity for intramuscular and even intravenous use, and it is believed that these are of considerable value in relapses.

The standardization of liver extracts is a question of great importance. The most reliable test now avaliabale is the change in the blood-picture in actual cases of pernicious anaemia. In view of the difficulty in securing early cases, the unsatisfactory condition of the assay can be seen. The ideal to be sought is some chemical assay, and, lacking that, a biological assay in which the unknown can be compared with a standard.

One point to be emphasized in the use of liver extracts is that they are not a complete equivalent of the whole liver from which they are derived. This is no doubt due to losses in various stages of the preparation. Hence the patients will need more extract than the amount of liver from which it is derived This fact is no doubt responsible for the occasional relapses due to the administration of insufficient extract to keep the blood picture at a safe level.

BOOK NOTES

Under the title, "Bedside Library for Students of Medicine," Professor Klotz has compiled a list of books, of which he says:

"Every student should have conveniently at hand some volumes of selected literature to be available for those occasional moments when diversion refreshes the mind, and for those last minutes before sleep closes the day's word. Fifteen or twenty minutes at the close of each day gives ample time to enjoy some fields of literature not too remote from the interests of the student of medicine. In preparing this list, it is assumed that each is familiar with his Bible and his Shakespeare."

For the benefit of those who have not the opportunity or occasion for perusal of the bulletin board near the door of the Pathological Reference Library, I am, with Professor Klotz's kind permission, reproducing here the list as it stands, hoping, particularly, that the students of the lower years will find it of use, and will avail themselves of its extremely interesting and valuable suggestion.

The Gold-headed Cane ..... MacMichael
The Great Physician . Edith Gittings Reid
or
The Life of Sir William Osler
Harvey Cushing
An Alabama Student ..... Osler
Aequanimitas ..... Osler
Religo Medici ..... Sir Thomas Browne
The Life of Pasteur ..... Vallery-Radot
The Breakfast Table Series.
Oliver Wendell Holmes
In Hospital ..... William Ernest Henley
The Moral Discourses ..... Epictetus
The Diary of Samuel Pepys.

There is a little book I have long wished to mention. It is "The Corner of Harley Street," written by H. H.

Bashford, distinguished man of medicine and letters. It consists of the letters of a successful physician to his children, his friends, his elderly, maiden hypochondriac aunt and others, and contains in it as much delightful humour, wise philosophy and sound advice as I have ever found within so small a volume. Too, there is much consolation to the student who forever struggles with mountains of almost meaningless names and crams into his head so much formidable memorization which will inevitably be crammed out again by the next lot. Anyone who should happen to borrow my copy will find, heavily underscored, certain passages which were as "balm in Gilead" during one hot summer when the shadow of a supplemental darkened many a sunny summer's day.

On the "New Book" shelf in the medical reading room there appeared recently a collection of essays carrying the title "Osler," by Dr. W. S. Thayer. The first few pieces centre about the great physician — about his work and his life in Baltimore, and constitute a charming addition to the rapidly accumulating "Osleriana." Dr. Thayer writes vividly and with a polished perfection of style that is rarely found in the literary efforts of a medical man. What he has to say — and there is much — is said in a manner that holds the reader's attention and draws him farther and farther into the pages of this delightful book. A.

THE UNIVERSITY OF MANITOBA MEDICAL JOURNAL.

All unbeknown, another undergraduate Medical Journal has been making its way into its third volume. The University of Manitoba Medical Journal appears to have been well established before its sister publication was aware of it. The present number (February, 1932) is a credit to the ranks of Canadian undergraduate medical journals. It consists of about thirty pages, and bears a striking resemblance to the University of Toronto Medical Journal, both in cover design, masthead and general outlay. We may either flatter ourselves that the Toronto magazine has been worthy of imitation, or that the adventurous editors who founded the Winnipeg journal independently reached the same results as did those who established this journal six years previously.

The articles are mainly by undergraduates: "Regulation of Blood Sugar," "B.C.G. for Infants," "Radium Therapy," "N.F.C.U.S.," with one article on "Spinal Anaesthesia," by a graduate. Editorials and alumni notes, and a loose page of medcial humour called "The Gore Pot" complete the number. The latter is evidently only sent to those whose characters are above reproach — thank you!

The paper and printing are excellent, and the contents are apparently the result of careful selection and much erudition.

We wish the University of Manitoba Medical Journal all success!

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VIOSTEROL SAFE IN PREGNANCY

USE OF VIOSTEROL DURING PREGNANCY

To the Editor:—Please advise me whether administration of irradiated ergosterol to pregnant women could cause a premature calcification of the fetal head, resulting in dystocia, with possibly damage later to the child.

M.D., Waco, Texas.

J.A.M.A., *Dec. 19, 1931*, *p. 1914*

ANSWER.—There is no danger to mother or child from therapeutic doses of viosterol (irradiated ergosterol) given during pregnancy. In fact, such medication probably would be of advantage, owing to the excessive drain of calcium and phosphorus that takes place during this period. This medication is especially indicated in cases in which the intake of calcium compounds has been insufficient.

MEAD'S VIOSTEROL IN OIL 250 D, because of its well-known effect upon calcium absorption, is attracting increased interest among obstetricians for use during pregnancy, especially in connection with foods rich in calcium, such as Mead's Cereal (220 mgm. Calcium per oz.). Aside from its mineral nutritional aspect, Mead's Viosterol in Oil 250 D has a marked effect in lowering blood coagulation time. Samples and literature on request. Mead Johnson & Company of Canada, Ltd., Belleville, Ontario. Pioneers in Vitamin Research.

Please enclose professional card when requesting samples of Mead Johnson products to cooperate in preventing their reaching unauthorized persons.

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A STATEMENT *regarding the Vitamin potency of* COD LIVER OIL CONCENTRATES

In view of claims being made by various manufacturers regarding the vitamin potency of Cod Liver Oil concentrates, the following points may be emphasized in connection with "Calcium A." which has stood the test of seven years' clinical experience.

(1) The concentrate used in its preparation is exhibited in an oil base enclosed in soft gelatin capsules. It has been our experience that its vitamin potency is much more satisfactorily preserved in oil which is the natural medium for the fat-soluble vitimins A and D.

(2) In addition to 70 milligrams of organically combined calcium and phosphorus, each "Calcium A" capsule contains 3,000 units Vitamin A (U.S.P.x) and 50 units Vitamin D (Steenbock). This approximates the vitamin value of one teaspoonful Ayerst Biologically-Tested Cod Liver Oil. The degree of concentration thus afforded is responsible for the satisfactory results obtained with "Calcium A." (*A more highly concentrated preparation is supplied in the form of Alphamettes which contain* 10,000 *units (U.S.P.-x) of Vitamin A and* 180 *units (Steenbock) of Vitamin D, thus representing over three teaspoonsful of Ayerst Cod Liver Oil*).

(3) "Calcium A" is an entirely Canadian product, and since it is intended for professional use, is marketed in keeping with professional dignity.

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